REMARKS

Initially, Applicants wish to thank Examiner Raymond for the courtesies he extended during the personal interview conducted on December 20, 2004, and his indication that Applicants' proposals for amending the claims would be favorably considered.

To expedite prosecution and to secure allowance at this time, applicants have cancelled claims 119-177, and have introduced claims 178-330. As discussed during the interview, all of these claims recite that the carrier comprises "Vitamin E TPGS". They also recite one or more specific co-solubilizers, which, in some claims, is/are further defined in terms of specific amounts based on the weight of the vehicle. The recited co-solubilizers are disclosed on pages 10-11 and 23 (shown in Table 2 as co-solubilizers with Vitamin E TPGS) of the specification, as well as in claims as originally filed. It is respectfully pointed out to the Examiner that certain of the claims presented herein were not presented at the interview. Thus, Applicants will specifically address all claim amendments.

Claims 178-243 and 330 are directed to compositions. Pursuant to the indication in paragraph 2 of the Office Action that the requirement for restriction is withdrawn, Applicants have introduced claims 244-329 directed to methods of treating a mammalian subject suffering from a taxane-responsive disease condition. The withdrawal of the restriction requirement is appreciated as well. The term "about" has been introduced into various independent claims to further define the amount of the carrier, for purposes of consistency with various dependent claims that further define the amount in terms of "about 30-90%". As far as other claims are concerned, claims 192, 212, 258 and 278 recite that the co-solubilizer is present in an amount of "50-70%" by weight of the vehicle, support for which is believed present in view of the disclosed ranges of "about

10-50%" and "about 0 to 70%". The recitations of "solution" and "suspension" in claims 213, 221, 279 and 287 are supported by the disclosure on page 12, lines 12-14 (and which serve to exclude the presence of water as would be present in an emulsion that is included in this disclosure). Claims 244-309 substantially correspond to claims 178-243. It is specifically pointed out that unlike claim 204, claim 270 does not recite that the composition is in "an oral dosage a hard or soft gelatin capsule." Claim 310-327 contain recitations set forth in claims 105-113 and 115-117. Claim 318 differs from claim 112 in that it also recites "inflammatory diseases", support for which is set forth on page 13, lines 4-5. Claim 320 differs from claim 114 in that it recites that the enhancing agent is orally administered in a separate oral dosage form, support for which is set forth throughout the specification beginning on page 13.

As agreed to during the interview in order to expedite prosecution of this patent application, aspects of Applicants' invention dealing with the two-part medicament, reflected in claims 42-52 and 94-104, as well as those aspects concerning compositions containing co-solubilizers other than the ones recited in the claims, or carriers other than Vitamin E TPGS, and methods of use thereof, will be pursued in one or more divisional patent applications.

In view of the foregoing, no new matter has been added. Therefore, entry of the amendment is respectfully requested.

Claims 119-177 have been rejected under 35 U.S.C. § 102(e) as anticipated by, or, in the alternative, under § 103(a) as obvious over U.S. Patent 6,458,373 to Lambert, et al. ("*Lambert*"). Applicants respectfully submit that in view of the cancellation of claims 119-177, these alternative rejections are rendered moot. Nonetheless, Applicants will address the

merits of *Lambert* to the extent to the extent it would be prospectively applied to claims 178-330 under either statute.

Each and every newly submitted claim is believed to be novel and nonobvious over the teachings of *Lambert*. *Lambert* does not teach or suggest pharmaceutical compositions containing a taxane, or a taxane derivative as an active agent, and a vehicle containing at least about 30% (or in some claims, at least 30% by weight) of Vitamin E TPGS, and the recited co-solubilizer(s), which in some claims is further defined in terms of specific amounts by weight of the vehicle.

More specifically, there is no disclosure or suggestion in *Lambert* of taxane compositions containing a taxane or taxane derivative as active agent, a vehicle containing (i) at least about 30% by weight of a carrier comprising Vitamin E TPGS, and (ii) a co-solubilizer comprising N-methyl-2-pyrrolidone, glycerol or propylene glycol esters of caprylic and capric acids, polyethylene glycol esters of caprylic and capric acids, saturated coconut and palm kernel fatty acids, or saturated polyglycolized glycerides, or oral administration of such compositions, to treat a mammalian subject, *e.g.*, a human, suffering from a taxane-responsive disease. See claims 229-243, 295-320, and 326-328. The Examiner's attention is also directed to the disclosures on pages 22-23 which indicate that such compositions unexpectedly achieve higher absorption levels compared to taxane compositions containing other carrier(s) and/or co-solubilizer(s).

Claims 238, 304, 328 and 330 each recites that the co-solubilizer further comprises ethanol. In addition to the arguments set forth above, *Lambert* teaches away from the use of ethanol, at least in terms of any functionally significant amounts. See, col. 4, lns. 6-18; col. 6, lns. 12-13; col. 11, lns. 1-2; col. 12, lns. 36-37 and col. 14, lns. 13-14. Moreover, working example 29 set forth on col. 23 illustrates

unpredictability with respect to formulating taxane compositions in ethanol and Vitamin E TPGS for purposes of oral administration.

There is no disclosure or suggestion in *Lambert* of taxane compositions containing a taxane or taxane derivative as active agent, a vehicle containing (i) at least 30% by weight of a carrier comprising Vitamin E TPGS, and (ii) a co-solubilizer comprising PEG 200 or PEG 400 in an amount of about 10-50% by weight of the vehicle. See claims 220-228, 286-294, 310-320, 325 and 327. For instance, the composition shown in example 10 (cols. 14-15) in *Lambert* is believed not to meet these recitations. In view of the unpredictability in the art, Applicants submit that it would not have been obvious to modify *Lambert's* composition to produce the claimed invention. In addition, it is explicitly taught for intravenous injection. See col. 15, lns. 16-21. Thus, the method claims are deemed not to have been obvious. On col. 9, lns. 65-67, *Lambert* also mentions polyethylene glycol as a secondary solvent, and on col. 10, lns. 13-17 as an ingredient of the aqueous phase. As pointed out herein, the disclosures on pages 22-23 indicate that the claimed compositions upon oral administration, unexpectedly achieve relatively high absorption levels. Such compositions may also achieve unexpected stability. Also, claims 221 and 287 are directed to solutions or suspensions, and thus exclude an aqueous phase. It would not have been obvious to modify *Lambert's* compositions to exclude the aqueous phase, since the invention is directed to an emulsion.

Claims 178-190, 194-203, 244-256, 260-269, 310-321 and 327 recite that the co-solubilizer comprises a lower molecular weight PEG, *e.g.*, PEG 200 or PEG 400, *and* ethanol. Although not all of these claims recited that the co-solubilizer is present in an amount of about 10-50% by weight of the vehicle, *Lambert* teaches away from the use of ethanol, at least in terms of any

functionally significant amounts. See, col. 4, lns. 6-18; col. 6, lns. 12-13; col. 11, lns. 1-2; col. 12, lns. 36-37 and col. 14, lns. 13-14. Moreover, working example 29 set forth on col. 23 in *Lambert* illustrates unpredictability with respect to formulating taxane compositions in ethanol and Vitamin E TPGS for purposes of oral administration.

There is no disclosure or suggestion in *Lambert* of taxane compositions containing a taxane or taxane derivative as active agent, a vehicle containing (i) at least about 30% by weight of a carrier comprising Vitamin E TPGS, and (ii) a co-solubilizer comprising propylene glycol, alone or in combination with ethanol. See claims 207-219, 273-285, 310-320, 323, 324 and 327. There are no working examples in *Lambert* teaching taxane compositions containing, *inter alia*, propylene glycol. On col. 10, lns. 16-17 and on col. 16, ln. 11, *Lambert* mentions that propylene glycol may be included as an ingredient of the aqueous phase. There is no teaching or suggestion of its use as a co-solubilizer, however, particularly in the amounts recited in various present claims. Aside from that, and as pointed out herein, the disclosures on pages 22-23 indicate that such compositions upon oral administration, unexpectedly achieve relatively high absorption levels. Such compositions may also achieve unexpected stability.

Applicants have also discovered that compositions wherein the co-solubilizer comprises propylene glycol *and* ethanol exhibit good stability and achieve unexpectedly high absorption upon oral administration. Recitations of the co-solubilizer comprising propylene glycol and ethanol are contained in claims 178-193, 198-203, 211-214, 217-219, 244-259, 264-269, 277-280, 283-285, 310-321, 324, and 327. On the other hand, as stated above, *Lambert* teaches away from the use of ethanol, at least in terms of any functionally significant amounts. See, col. 4, lns. 6-18; col. 6, lns. 12-13; col. 11,

lns. 1-2; col. 12, lns. 36-37 and col. 14, lns. 13-14. Moreover, working example 29 set forth on col. 23 illustrates unpredictability with respect to formulating taxane compositions in ethanol and Vitamin E TPGS for purposes of oral administration.

There is no disclosure or suggestion in *Lambert* of taxane compositions containing a taxane or taxane derivative as active agent, a vehicle containing (i) at least about 30% by weight of a carrier comprising Vitamin E TPGS, and (ii) a co-solubilizer comprising ethanol in an amount of about 10-50% by weight of the vehicle, which is in an oral dosage form of a hard or soft gelatin capsule, or oral administration of such a composition (not necessarily in capsule form) to treat a mammalian subject *e.g.*, a human, suffering from a taxane-responsive disease. See claims 204-206, 270-272, 310-320, 322, 327 and 329. Example 29 on col. 23 of *Lambert* does not explicitly teach the claimed composition which is in an oral dosage form of a soft or hard gelatin capsule (*i.e.*, *Lambert* states that suitability for oral administration was "simulated"). In addition, since *Lambert* determined that this composition was "not suitable for oral administration of paclitaxel," this publication teaches away from use of the claimed composition for oral administration (and thus from actually formulating the composition into a soft or hard gelatin capsule or any other oral dosage form).

In view of the foregoing, Applicants submit that the presently claimed invention is novel and nonobvious over *Lambert*. Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

Lastly, the indication in paragraph 1 of the Office action is acknowledged. During the interview, the Examiner reiterated that Applicants' prior arguments on this issue were

convincing to withdraw rejections based on obviousness-type double patenting.

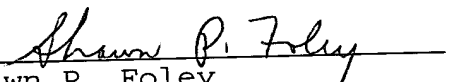
As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: December 29, 2004

Respectfully submitted,

By 

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